UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/583,591	06/19/2006	Simon L. Stubbs	PA0394	4011

22840 7590 08/10/2010

GE HEALTHCARE BIO-SCIENCES CORP.
PATENT DEPARTMENT
101 CARNEGIE CENTER
PRINCETON, NJ 08540

EXAMINER	
MONSHIPOURI, MARYAM	
ART UNIT	PAPER NUMBER
1656	

NOTIFICATION DATE	DELIVERY MODE
08/10/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

LSUSPatents@ge.com

Office Action Summary	Application No.	Applicant(s)	
	10/583,591	STUBBS ET AL.	
	Examiner	Art Unit	
	MARYAM MONSHIPOURI	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 June 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,12-15,21-38,43,46 and 47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,12-15,21-38,43,46 and 47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/19/06*.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *5/27/10* .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicant's response to restriction requirement of 10/15/09 and his/her supplementary amendment of 6/2/10 are acknowledged. Applicant elected Group I (original claims 1-38 and 41) and Group (j), a cytochrome C with a single mutation at position 72 or DNA encoding it.

In supplemental amendment of 6/2/10, applicant canceled claims 5-11, 16-20, 39-42 and 44-45.

DEATLED ACTION

Claims 1-4, 12-15, 21-38, 43 and 46-47 are under examination on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 14 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Said claim depends from claim 12 which recites numerous fluorescent proteins. it is unclear, whether all said fluorescent protein shave identical amino acid sequences and if not, which reference (base) amino acid sequence is utilized for claim 14 (i) to (iii). Appropriate clarification is required.

Claim 1-4, 12-15, 21, 23-38, 43 and 46-47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear if in claim 1(a) modified cytochrome C is restricted to human source or can be from other or additional sources. Applicant is well aware that some extensively modified SEQ ID NO:2

derivatives may eventually read on the amino acid sequences of for example horse or Drosophila cytochrome C etc.. appropriate clarification is required.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4, 12-15, 21-38, 43 and 46-47 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The phrase " wherein said modified cytochrome C comprises the amino acid substitution selected from the group consisting of K73A, K73L, K73R, K73G and K73X, wherein X represents trimethylation" in claim 1 and its dependent claims 2-4, 12-15, 21, 23-38, 43 and 46-47 and claim 22 do not seem to have any support in the disclosure and is considered to be **new matter.** In his/her amendment of 6/2/10 applicant mentions that it is convention in the prior art (see for example, Yu et al., JBC, 276(16), 13034-13038, cited in the IDS) to eliminate the N-terminal lysine of cytochrome C before numbering its amino acid sequence. However, since instant claims refer to the entire amino acid sequence of human cytochrome C (i.e. SEQ ID NO:2 in the sequence listing), residue 72 as recited in original claims 5-8 should be renumbered as residue 73 (as done in instant amendment) and no new matter is introduced in the claims or disclosure.

This explanation is **unpersuasive**. If in fact, as applicant mentions, numbering of cytochrome C is conventionally done differently in the prior art it is unclear why applicant had not adopted said "conventional" numbering at the time of filing of this application. It is also unknown why this discrepancy in cytochrome C amino acid numbering was not even mentioned anywhere in the disclosure. Applicant is advised to provide support for the above mentioned phrase in response to this office action or possibly delete said phrase from base claim 1.

In case applicant provides support for the phrase above, recited in claim 1, the following rejection may apply:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-38 and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Los et al. "Los" (WO 02/08752, 1/2002, cited in the IDS) in view of Evans et al. "Evans" (Uniprot database, accession No.P9999, 1986, see also hit #2 of Uniprot sequence search results, under PAIR) further in view of Kluck et al. "Kluck", (JBC, 275(21), 16127-16133, 2000, cited in the IDS). Los teaches preparation of cytochrome C (cyt C) fused to fluorescent reporters and a method of modulating its transport for detecting cell apoptosis. Los does not teach any recombinant cyt C fusion product

wherein residue 72 of N-terminal truncated cyt C (corresponding to residue 73 of instant SEQ ID NO:2) is substituted or trimethylated.

Evans teaches the nucleotide sequence of human cyt C and Kluck teaches that post modification of lysine 72 of N-truncated cyt C (corresponding to residue 73 of instant SEQ ID NO:2) could result in its inactivation of caspase mediated apoptotic pathway through its declined or diminished affinity for Apaf-1.

At the time the invention was made it would have been obvious to one of ordinary skill I the art to start with the fusion product of Los and prepare a recombinant version thereof ,utilizing the DNA sequence of Evans, wherein lysine residue 72 (corresponding to residue 73 of instant SEQ ID NO:2) is trimethylated as taught by Kluck. One of ordinary skill in the art is motivated in preparing such modified cyt C fusion product because said product could be tested for its pro-apoptotic activity in a method that determines the localization of said recombinant modified fusion construct within the host cell, wherein a change in localization in said cell is indicative of apoptosis. Obviously modulating the activity of such recombinant fusion product would eventually lead to identification of drugs that for example, lower unwanted apoptosis in patients with inflammation etc. Such modified cyt C fusion product would also inherently have at least, 10, 100 or a 1000 times less affinity for Apaf-1 by inherency.

One of ordinary skill in the art has a reasonable expectation of success in preparing the modified cyt C fusion product of Los in view of Evans, further in view of Kluck because methods of preparing such fusion products are merely routine in the prior art, rendering the invention obvious.

Applicant is reminded that the types of fluorescent proteins (or mutants thereof) used in the construct (see claims 12-15) as well as the types of promoters and vectors utilized for recombinant expression of said modified cyt C fusion product (see claims 23-37) cannot be considered to be contribution over the prior art in view of the art cited above.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARYAM MONSHIPOURI whose telephone number is (571)272-0932. The examiner can normally be reached on Tues.-Fri., from 7:00 a.m to 5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Rao Munjunath can be reached on (571) 272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Maryam Monshipouri/

Primary Examiner, Art Unit 1656

***